

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization International Bureau



554294

(43) International Publication Date
11 November 2004 (11.11.2004)

PCT

(10) International Publication Number
WO 2004/096788 A1

(51) International Patent Classification⁷: **C07D 309/00**, (74) Agent: HABETS, Winand, Johannes, Petrus; Intellectual Property, P.O. Box 9, NL-6160 MA Geleen (NL).

(21) International Application Number: PCT/NL2004/000284

(22) International Filing Date: 28 April 2004 (28.04.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data: 03101227.1 2 May 2003 (02.05.2003) EP

(71) Applicant (for all designated States except US): DSM IP ASSETS B.V. [NL/NL]; Het Overloon 1, NL-6411 TE Heerlen (NL).

(72) Inventors; and

(75) Inventors/Applicants (for US only): MINK, Daniel [DE/BE]; Heckenweg 5, B-4700 Eupen (BE). WOLBERG, Michael [DE/DE]; Römerstrasse 99b, 52428 Jülich (DE). BOESTEN, Wilhelmus, Hubertus, Joseph [NL/NL]; Brountselaan 9, NL-6132 BJ Sittard (NL). SEREINIG, Natascha [AT/NL]; Gabriel Metsulaan 92, NL-5611 SR Eindhoven (NL).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 2004/096788 A1

(54) Title: PROCESS FOR THE PREPARATION OF (4-HYDROXY-6-OXO-TETRAHYDROPYRAN-2-YL) ACETONITRILE AND DERIVATIVES THEREOF

(57) Abstract: The invention relates to a process for the preparation of (4-hydroxy-6-oxo-tetrahydro-pyran-2-yl)-acetonitrile from 6-X-substituted-methyl-4-hydroxy-tetrahydro-pyran-2-one, wherein X stands for a leaving group, by reacting 6-X-substituted-methyl-4-hydroxy-tetrahydro-pyran-2-one with a cyanide ion in water and by subsequent lowering of the pH to a pH between 0 and 5. (4-hydroxy-6-oxo-tetrahydro-pyran-2-yl)-acetonitrile and other compounds obtainable from (4-hydroxy-6-oxo-tetrahydro-pyran-2-yl)-acetonitrile may suitably be used in the preparation of a pharmaceutical preparation, more in particular in the preparation of statins, more in particular in the preparation of Atorvastatin or a salt thereof, for instance its calcium salt. The invention also relates to (4-hydroxy-6-oxo-tetrahydro-pyran-2-yl)-acetonitrile and other compounds obtainable therefrom.